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Dear Joe:

Just some further thoughts on screening programs-- voicewriter happens to be in use elsewhere.

1. "Anti-Glucose". I just remembered that there already has been some work on L-sorbose that points in this direction (Cf. Tatum, Science, May 20,1949). Quite possibly, the reversal by glucose is by competing for the penetration of the inhibitor, which leaves the principle intact. I don't think that sorbose is appreciably inhibitory on E. coli (growth on glucose), but I haven't tested its effect on glycolysis (yet). -- PS no effect on coli.

2. Antiviral screening. I hear several companies are abandoning their programs. I am beginning to think myself that one of the most vulnerable aspects of the virus may be its "penetration reaction", i.e., the splitting of NA from protein, which normally occurs at the surface of the host cell. If the NA is split in vitro, the virus becomes, of course noninfective. The point is that phage, e.g, can be split in pyrophosphate at certain pH's, and also on glass in the presence of tryptophane (Puck), as well as by osmotic shock and by bacterial wall fragments. It might be possible to find other agents with comparable activity more suitable for therapeutic purposes. Frankly, it might be better to set up a chemical rather than a biological test-- e.g., for the release of nonsedimentable or DNAase-accessible DNA (or cf. RNA) from phage, TMV or an animal virus. If any of the latter can be readily procured by you in moderate quantitities, there would be a real opportunity.

This notion leads to another possibility, the elective enrichment of soil microflora that would be able to persist on purified virus preparations, which would imply that they could denature and split the virus.

3. Protocol for effects on crossing in E. coli. As I thought about this, it seemed to me it could be reduced to such a simple scheme that you might like to hear about it. If Hfr M- Lac+ is cross-brushed against F-Lac- (Prototroph) on a medium we call "M/Lac" (= EMS Lac without succinate), crossing is very readily detected by the development of several hundred small, but prominently colored, Lac+ Prptotrophic recombinants in the region of cross-streaking. The streaks are made from broth, and no washing is needed. F+ x F- under comparable conditions gives 10-20 colonies. The protocol I would suggest would be to grow Hfr, F+ and F- each in separate broth tubes (1 or 10 ml) to which substances X are added, then cross-brush the Hfr and F+ against the F-. About 10 such groups of tests can be made on one plate (which should include a control) so not much work is involved. The procedure should pick up any effect that diminishes or enhances the activity of Hfr or F+, or on the F-; I would judge it better to treat all of the components in the crosses. Of course, antibacterial action of X would probably be already known, and be relatively uninteresting in this context.

4. Protocol for transduction: rather similar to above, but I would incubate sample of HFT phage (see Genetics, Jan 56) as well as of Gal- bacteria with X, then cross-brush, also on "M/Gal" (to minimize residual growth of Gal- recip.)

HFT lysates can be diluted 10:1 or 100:1 and still give readable reactions in cross-brushes of loopful amounts. To date, we know of no agent that will inactivate transducing activity except heat (and probably formaldehyde and some similar corrosives) but have not tested extensively. Transducing activity is far more resistant than (to UV) the phage ~~to UV~~ (qua plaques). The "splitting reaction" undoubtedly would inactivate HFT lambda.

Your only problem here would be in maintaining heterogenotes, and obtaining HFT lysates for routine use. By using a balanced heterogenote, e.g., $Gal_2^-/ex\ Gal_4^-$ (the ex marks the "exogenote" or fragment) (in which galactose-positive colonies are almost invariably heterogenotic) you should be able to maintain a reliable HFT source; I think you have had enough background in inducing lambda to be able to manage the rest of it without much trouble.